Remarks

Amendment to Specification

The specification has been amended in order to incorporate the revised sequence listing into the application. The amendment does not add new matter.

Sequence Listing

Applicants have enclosed a revised sequence listing and have made the necessary request that it be incorporated into the specification. The sequence listing is believed to comply fully with the sequence listing rules. Under EFS-Web filing procedures, Applicants believe that they need to submit only an electronic version of the sequence listing in order to comply with the pending Notice.

The revised sequence listing submitted herewith addresses the issues listed in the raw sequence listing error report referenced in the Office Action. The sequence listing adds no new matter and applicants respectfully requests its entry.

The Claim Amendments

Claims 1, 3, 14-21, 30, and 35 have been amended and claims 2, 4-13, 22-29, and 31-34 have been previously canceled. New claims 36-39 have been added. Applicant has amended claim 1 so that it is drawn to a chemically modified nucleic acid molecule having the following features: (1) it comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides; (2) each strand of the nucleic acid molecule is independently 18 to 27 nucleotides in length; (3) the antisense strand of the nucleic acid molecule comprises 18 to 27 nucleotides that are complementary to a VEGFr1 and VEGFr2 RNA comprising SEQ ID NOs: 2752 and 2753 respectively; (4) the sense strand of the nucleic acid molecule is complementary to the antisense strand, and comprises an 18 to 27 nucleotide portion of the VEGFr1 and VEGFr2 RNA sequence; (5) about 50 to 100 percent of the nucleotides in the sense strand and about 50 to 100 percent of the nucleotides in the antisense strand of the nucleic acid molecule are chemically modified with modifications independently selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and (6) one or more of the purine nucleotides present in one or both strands of the nucleic acid molecule are 2'-O-methyl purine nucleotides and one or more of the pyrimidine nucleotides present in one or both strands of the nucleic acid molecule are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

Amended claim 1 is fully supported by the specification as filed, for example, inter alia, at pages 13 (lines 6-10), 13 (lines 11-25), 15, 17, 20-23, 25-26, 34-36, 36 (lines 20-22), 42-45, 165, and 177. Support is also found in the priority documents U.S. Provisional patent application Nos. 60/363,124 (see, page 10, lines 3-20, page 12, lines 4-6, page 285 and page 416), 60/440,129 (see, page 7, lines 23-30, page 8, lines 5-11), and PCT US03/05022 (see pages 6-9, 12-13, 14, 15, 16, 20, 21, 22, 31-34, 37-42, 149, and 161).

In addition, claims 14, 15, 18, 19, and 20 have been amended to clarify that 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the specified purine or pyrimidine nucleotides has the specified modification. Support for the amendment is found in the specification at, for example, pages 34-36. Support is also found in the priority documents. See, e.g., U.S. Provisional patent application No. 60/440,129 (see, page 10, lines 10-17, page 15, lines 4-20, page 22, lines 1-9 and lines 25-30, page 23, lines 15-20, and page 25, lines 20-25). See, e.g., U.S. Provisional patent application Nos. 60/363,124 (see, page 10, lines 3-16 and page 11, lines 1-11) and PCT US03/05022 (see pages 31-34).

In addition, the claims have been further amended merely to correct dependencies and other matters of form.

New claim 36 recites a chemically modified nucleic acid molecule, wherein the molecule is chemically modified with one or more phosphorothioate internucleotide linkage, 2'-O-methyl ribonucleotide, 2'-deoxy-2'-fluoro ribonucleotide, 2'-deoxy ribonucleotide, universal base nucleotide, 5-C-methyl nucleotide, inverted deoxyabasic or any combination thereof. Support for new claim 36 can be found in the specification at, for example, pages 17, 25-26 and 42-45. Support is also found in the priority documents. See, *e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*see*, page 5-8, 10, and 11) and 60/440,129 (*see,* page 15, lines 14-20 and page 10, lines 10-13). See, e.g., PCT US03/05022 (pages 14, 37-38, and 41-42).

New claim 37 recites a double stranded nucleic acid wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the sense strand are 2'-O-methyl pyrimidine nucleotides. Support for new claim 37 can be found in the specification at, for example, pages 34-36. Support is also found in the priority documents. See, *e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*see*, page 10, lines 3-16) and 60/440,129 (*see,* page 15, lines 14-20 and page 10, lines 10-13). See, e.g., PCT US03/05022 (pages 31-34).

New claim 38 depends from claim 19 and recites a double stranded nucleic acid molecule wherein additionally 1, 2, or 3 purine nucleotides in the sense strand are 2'-O-methyl nucleotides. Support for new claim 38 is found in the specification at, for example, pages 34-36. Support is also

found in the priority documents. See, e.g., U.S. Provisional patent application No.60/440,129 (see, page 25, lines 20-25, page 10, lines 13-17). See, e.g., PCT US03/05022 (pages 31-34).

New claim 39 depends from claim 1 and recites a method of inhibiting the expression of VEGFr1 and VEGFr2 comprising administering the nucleic acid molecule of claim 1 to a human subject in need thereof under conditions that allow for inhibition of VEGFr1 and VEGFr2 expression. Support for new claim 39 is found in the specification at, for example, pages 14-15 and 51-57, as well as in PCT US03/05022 (48-53) and U.S. Provisional patent application No. 60/343,124 (pages 15-18).

New claim 40 recites a nucleic acid molecule, wherein the antisense strand, sense strand, or both the antisense strand and sense strand comprise a 3'-overhang of 1-3 nucleotides. Support for new claim 34 is found in the specification at, for example, page 20 as well as in PCT US03/05022 (14 and 17) and U.S. Provisional patent application No. 60/343,124 (pages 4, 5, and 9).

New claim 41 depends from claim 34 and recites a nucleic acid molecule wherein the nucleotides of the 3'-overhang are chemically modified. Support for new claim 34 is found in the specification at, for example, page 20, as well as in PCT US03/05022 (14 and 17) and U.S. Provisional patent application No. 60/343,124 (pages 4, 5, and 9).

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections and are fully supported by the specification as filed. Additionally, these amendments are not an admission regarding the patentability of subject matter of the canceled or amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application. The amendments add no new matter and applicants respectfully request their entry.

A complete listing of all the claims, in compliance with the revised amendment format, is shown above.

Priority

The Office accords the instant application a priority date of January 12, 2004, which is the filing date of the application. The Office did not accord the instant application the benefit of the earlier priority applications because it alleges that support for the claims, specifically GenBank Accession Number NM_002019 (SEQ ID NO: 2752) and GenBank Accession Number NM_02253 (SEQ ID NO: 2753), is not readily apparent in the priority documents. The Office further states that neither the instant application nor the priority documents provide support for a molecule wherein each strand is independently about 14 to 28 nucleotides in length.

Applicant submits that the instant application claims priority, *inter alia*, to PCT/US03/05022, which claims the benefit of U.S. provisional applications 60/363,124 and 60/440,129. Both PCT/US03/05022 and provisional application 60/363,124 fully support a nucleic acid molecule comprising a sense and antisense strand targeted to VEGFr1 and VEGFr2 RNA sequences, for example, the sequences found in GenBank Accession Nos. NM_002019 and NM_002253. PCT/US03/05022 provides support for GenBank Accession No. NM_002019 (SEQ ID NO: 2752) at Tables I and II of the specification and GenBank Accession No. NM_002253 (SEQ ID NO: 2753) at Tables I and II of the specification. U.S. Provisional application 60/363,124 provides support for GenBank Accession No. NM_002019 (SEQ ID NO: 2752) at page 416 of the specification and GenBank Accession No. NM_002253 (SEQ ID NO: 2753) at page 285 of the specification.

Support for the other claim elements are found in PCT/US03/05022 and U.S. Provisional application 60/363,124, as provided herein above.

The Office alleges that the support must exist in each of the intervening documents. However, Applicant submits that each of the applications listed in the priority claim are incorporated by reference and thus contain the support discussed above via proper incorporation by reference. Applicant notes that MPEP 608.01(p) states that the limitations on the material which may be incorporated by reference in U.S. patent applications do not apply to applications relied on only to establish an earlier effective filing date under 35 U.S.C. 119 or 35 U.S.C. 120. Neither 35 U.S.C. 119(a) nor 35 U.S.C. 120 places any restrictions or limitations as to how the claimed invention must be disclosed in the earlier application to comply with 35 U.S.C. 112, first paragraph. Accordingly, an application is entitled to rely upon the filing date of an earlier application, even if the earlier application itself incorporates essential material by reference to another document. See *Ex parte Maziere*, 27 USPQ2d 1705, 1706-07 (Bd. Pat. App. & Inter. 1993).

Double Patenting

The Office has maintained the Obviousness-Type Double Patenting rejection of claims 1, 3, 14-23, 32 and 35 over claims 1-30 of copending Application No. 10/664,668 and claims 49-51 and 58-76 of copending Application No. 10/444,853. Applicant reiterates that it will consider filing a terminal disclaimer upon allowance of the pending claims.

Claim Objections

The Office objects to claim 3 because it allegedly fails to further limit the subject matter of a previous claim. Specifically, the Office states that claim 3 fails to further limit claim 1 because it recites an siRNA molecule comprising ribonucleotides and siRNA molecules necessarily comprise ribonucleotides. Applicant has amended claim 1 to recite a "nucleic acid molecule", thereby obviating the objection. Accordingly, Applicant respectfully requests withdrawal of the claim objection.

35 USC §112, Second Paragraph, Rejection

Claims 1, 3, 14-23, 32, and 35 have been rejected under 35 USC §112, second paragraph, as allegedly being indefinite because claim 1 recites VEGFr1 and VEGFr2 as each corresponding to SEQ ID NO: 2752. Applicant has amended claim 1 to recite that VEGFr1 comprises SEQ ID NO: 2752 and VEGFr2 comprises SEQ ID NO: 2753, thus rendering the rejection moot. Applicant respectfully requests withdrawal of this 35 §112, second paragraph, rejection.

35 USC §112, First Paragraph, Rejections

Written Description/New Matter

Claims 1, 3, 14-23, 32, and 35 have been rejected under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Office states that claims 1, 3, 14-23, 32, and 35 are directed to a chemically modified double stranded siRNA molecule wherein each strand is independently "about 14 to 28 nucleotides in length" and the antisense strand comprises "about 14 to 28 nucleotides in length that are complementary" to SEQ ID NO: 2752 or a portion thereof. The Office argues that the instant specification does not support the claim elements wherein the length of each strand is "about 14 to 28 nucleotides in length" and the antisense strand comprises "about 14 to 28 nucleotides that are complementary" to SEQ ID NO:2752 or a portion thereof. The Office further argues that the specification does not teach that both VEGFr1 and VEGFr2 correspond to the same sequence, SEQ ID NO: 2752, as instantly recited.

In response, Applicant submits that the claims have been amended to recite that each strand of the nucleic acid molecule is independently 18 to 27 nucleotides in length wherein the antisense strand comprises 18 to 27 nucleotides that are complementary to a vascular endothelial growth factor receptor 1 (VEGFr1) RNA sequence comprising SEQ ID NO: 2752 and vascular endothelial growth factor receptor 2 (VEGFr2) RNA sequence comprising SEQ ID NO: 2753. In addition, the claims

have been amended to recite that the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide portion of the VEGFR1 and VEGFR2 RNA sequence.

The amendments are fully supported in the specification. The specification teaches that the nucleic acid molecules comprises an antisense strand and sense strand 18 to 27 nucleotides in length at, for example, page 36. The specification teaches that the antisense strand is complementary to a vascular endothelial growth factor receptor 1 (VEGFr1) RNA sequence comprising SEQ ID NO: 2752 and vascular endothelial growth factor receptor 2 (VEGFr2) RNA sequence comprising SEQ ID NO: 2753 at, for example, pages 13, 165, and 177. The specification teaches that the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises a portion of the VEGFR1 and VEGFR2 RNA sequence at, for example, page 13.

Applicant submits that the claims, as amended, are fully supported by the instant specification. Accordingly, Applicant respectfully requests withdrawal of this 35 §112, first paragraph, rejection.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, she is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

Dated: June 18, 2007

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